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TI **Peptoid**-based foldamers: Application of synthetic, sequence-specific polymers for biological mimicry of lung **surfactant** proteins.
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AB -Foldamers' are non-natural, sequence-specific oligomers designed to mimic the folding properties of natural polypeptides. We are designing protein mimics that are based on a class of synthetic, sequence-specific foldamers called -polypeptoids,' i.e., N-substituted glycine polymers, whose advantages for biol. mimicry include their ease of synthesis, protease stability, and low immunogenicity. Using automated solid-phase synthesis, we produce polypeptoids with specific sequences of biomimetic, proteinogenic sidechains. Despite an absence of chiral centers and hydrogen-bond donors in the polymer backbone, some polypeptoid sequences adopt stable helixes in soln. that exhibit intense CD spectra resembling those of peptide alpha-helixes. Along with studying the folding propensities of biomimetic polypeptoids, we have focused on designing **peptoid**-based mimics of the helical lung **surfactant** proteins SP-B and SP-C, as safe, bioavailable alternatives to animal-derived **surfactants**. Whereas natural SP-C peptide misfolds and aggregates in soln., **peptoid**-based, helical SP mimics are stable in soln. and show promising biophys. properties as detd. by CD, surfactometry, and fluorescence microscopy.